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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,208	10/27/2005	Mezher Hussein Ali	AC-21-US	3691

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
06/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,208	ALI ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-30* is/are pending in the application.

4a) Of the above claim(s) *15-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

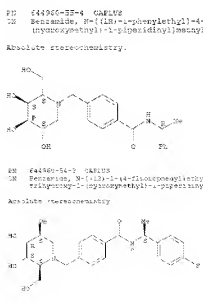
1. Amendment and response filed by applicants dated Mar. 13, 2009 have been entered and considered carefully.

Claims 1-11, 13-14 are pending. Claims 15-30 stayed withdrawn from consideration per 37 CFR 1.142(b).

2. Applicants' continuous argument with respect to the restriction requirement has been noted. The restriction has been made final.

3. The rejection of claims 1-10, 13-14 under 35 USC second paragraph is maintained for reason of record.

It has been clearly delineated in the previous office action that the CAS clearly provided the standard in nomenclature of compounds with enantiomeric/optical isomers.
Both the "---" and the "◄" together with the explicit "S" or "R" are needed for proper identification of the specific isomer. It was in the record that CAS employed both symbol and letter to clearly identify the stereo isomers i.e.:



It is not understood as to what was the attorney is arguing about. If the attorney is arguing that the claimed compounds are explicit steroisomers then there is no good reason why the CAS nomemclature should not be adopted, since the "S" or "R" identification together with the "---" and the "◄" will clearly naming the compound, i.e. meeting the particularity required under the second paragraph. If attorney is arguing that it should let one having ordinary skill in the art to interpret, i.e. recited on pages 13-15 of the response, therefore the "---" and the "◄" can be either "S" or "R" decided by the reader, then, the 102 anticipation is proper and will be maintained in following sections.

4. The rejection of claims 1-11, 13-14 under 35 USC 112 first paragraph for lacking sufficient enablement with respect to the "prodrug" is maintained for reason of record.

The internet definition of "prodrug" is hereby attached for applicants' convenience. It is clearly stated that the prodrug is "not active" and the drug activity is release only after metabolic conversion of the prodrug to the "drug".

It is not understood what was the attorney arguing with respect to the statement that:

> *"Page 5, paragraph [0105] of the published specification (2006/0058349) provides that"[s]uitable prodrugs of the compounds of formula (I) include, but are not limited to,pharmaceutically acceptable esters such as C_{1-4} alkyl esters." As such, the specification enables one skilled in the art to make and use C_{1-4} alkyl esters of formula (1) as a prodrug without undue experimentation" (p.15 3/13/09 response)*

Does it mean that the term "prodrug" is referring to C_{1-4}alkyl ester of formula I or does it mean all prodrugs are enabled? Please note that to the extend, the prodrugs are referring to acylated modification of the functional groups of formula I, similar compounds have been shown that both free hydroxyl and acylated hydroxyl compounds having biological activity (see US 5,003,072 col. 21, table 1). Therefore, the acylated compounds are not "inactive" prodrugs of the non-acylated compounds.

Nowhere in the specification described or enabled a prodrug-drug relationship as to enable one having ordinary skill in the art to practice the scope as claimed.

5. The rejection of claims 1-10, 13-14 under 35 USC 102(b) over Boeshagen et al. CA 113:126581, see RN attached; Ezure et al. CA 116:236093, RN 141206-38-4; Broek et al. CA 119:96007, RN 149302-52-3, RN 149302-53-4; Berg et al. RN 8117-43-3; Kurihara et al. CA 114:185939 RN 133342-47-9 is maintained for reason of record since the claims are not "S" or "R" limited using only the up and down notation (see supra section 3).

6. The rejection of claims 1-11, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boshagen et al. US 5,051,407 or the rejection of claims 1-11, 13-14 over Jacob US 6,225,325 in view of Greene are maintained for reason of record.

The gist of applicants argument is that in addition to the difference in substitution, there are stereo configuration difference between the prior art compounds and the claims. Please note that applicants are arguing that applicants are arguing that "---" and the "◄" can be decided by the reader and are not be limited to the specific "S" or "R" configuration. Applicants must decide if the claims have the explicit particularity in the configuration of "---" or the "◄" is explicitly corresponding to a specific "S" or "R" configuration or not. If with the particularity, the claimed compounds are demarcated from the prior art variation, then such difference can be considered. Please note that in section 3, it was clearly evidence that both up and down at the 2 and 5 position are 2S and 5S.

In addition, applicants argued that in the court has held dextrorotatory and levoratarory enantiomers patentable based on *favorable antiplatelet activity bot with no significant neurotsocicity* of the dextrorotatory isomer (Snofi v Apotex p.18 of response). Applicants then quoted the Kato et al. reference which showed variations of biological activities of the different enantiomeric azasugars. Please note that Kato et al. at p.2036 introduction stated that:

> *"Azasugars (or iminosugars) are an important class of glycosidase inhibitors and are arousing greatinterest as potential therapeutic agents such as antidiabetics, antiobesities, antivirals, and therapeutic agents for some genetic disorders".*

Kato et al. is describing the general *state-of-the-art*, even though the reference is published in 2005, the introductory statement were based on references 1-5 published before 2003. MPEP 2164.05(a) permit the use of late publication to show what was known to one having ordinary

skill at the time invention was made. In addition, similar state-of-the-art statement were found for example in US 5,276,120 col. 2 lines 9-25. In other words, "deoxyazasugar" is known as a "*class*" of compounds with biological activity. Deoxyazasugars therefore is referring to iminosugars with all the stereo-configuration of the naturally occurring "saccharides". This very conventional teaching is referring to that when a lead deoxyazasugar is found with biological activity, one can modify the stereo-configuration with other saccharides with the expectation that it will have biological activity. Of course, different saccharides having different stereo-configuration would display variation of activity innately (see introduction p.2037 left column, or similarly col. 2-4 '120). Applicants further argued that the prior art compounds showed variation of biological activity and do not *all* have the GCS inhibitory activity. Please note that, the modification of each conventional species is for the *disclosed* biological activity for that species, such activity does not have to be identical to applicants' utility. In addition, obviousness to modify does not require absolute predictability of the outcome just reasonable expectation. In re Kronig 190 USPQ 425; Ex parte Erlich 3 USPQ2d 1011. Therefore, if there are variation of biological activity, it does not negate the finding of obviousness as delineated for the compounds in the previous office action. It is immaterial that applicants' utility may differ from that of the art (please note that the rejections are on the compounds). Arguments regarding different utility must be based on a meaningful showing of an unexpected difference in properties of applicants' compounds versus the compounds of the prior art. In re Hoch 166 USPQ 406; In re Payne 203 USPQ 247. In the Sanofi v Apotex decision recited by applicants it was the "factual difference" in neurotoxicity that demarcated the two enantiomers on patentable merits.

In the instant case, it was evidenced in analogous art that variation of stereo structure of the piperidine core would not affect the activity and are alternative choices for such compounds (see especially, US 7,250,005 col. 7-8) and Kato et al. disclosed the same expectation that all enantiomers are biologically active while some may be more active or selective than others against specific enzymes (see 12/11/08 office action p.6). Applicants provided mere argument with respect to utility without any factual support that the prior art compound is devoid of the

instant utility. Mere argument with respect to variation without factual support is entitled to little weight. In re Lindner 173 USPQ 356.

7. The provisional rejection of claims 1-11, 13-14 under the judicially created doctrine of obviousness type double patenting over copending Application No. 10/522,207 or 10/586,188 in view of US 5,051,407 or US 7,250,005 and Kato et al. is maintained for reason of record.

The same explanation supra is also applicable here. Applicants neither demarcated the scope of the copending claims nor filed acceptable terminal disclaimer.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Jun. 1, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625